

In the Specification

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10/4/04

Please substitute the following paragraph on page 4, beginning at line <sup>14</sup>15:

- 1) Resolve *dl*-*threo*-methylphenidate by the procedure described in the Example of PCT/GB97/00185 (International Publication No. WO 97/27176): Ditoluoyl-D-tartaric acid (5.033 g, 12.4 mmol) was suspended in a solution of 2% methanol in acetone (10 ml), and a solution of *threo*-methylphenidate (2.9 g, 12.4 mmol) in the same solvent (10 ml) was added. The solution was gently warmed to reflux whereupon all the reagents dissolved. The solution was immediately cooled and crystals began to form. The solution was allowed to stand at 4°C for 17 hours and was then filtered. The crystals were washed with acetone (3 x 15 ml) and dried *in vacuo* to yield the ditoluoyl-D-tartrate salt of *d*-*threo*-methylphenidate (3.516 g, 44.3% by weight; corresponding to 97% ee *d*-*threo* methylphenidate, as determined by chiral HPLC after salt cracking). The mother liquors were dried *in vacuo* to yield the ditoluoyl-D-tartrate salt of *l*-*threo*-methylphenidate as a solid, dry form (4.508 g, 50.5% yield, 88% ee).

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The ditoluoyl-D-tartrate salt of *d*-*threo*-methylphenidate (3.486 g), obtained as described above, was suspended in 2% methanol in acetone, and warmed to c. 40°C and cooled. This did not dissolve the solid which was stirred at room temperature for 24 hours. The suspension was filtered, the solid washed with acetone (10 ml) and dried *in vacuo*, to yield diastereomerically pure material (3.209 g, 92% recovery, corresponding to >99% ee *d*-*threo*-methylphenidate).

Repeating this protocol using isopropanol: methanol as the solvent, gave the same salt, on initial crystallization, enriched in at least 98%. Reslurrying increased this.